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EXAMINATION OF THE HEART IN INDUSTRY*

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IN considering heart examination in industry it has seemed to me that we would best use the time allotted to us if we considered not the details of such an examination itself, but rather what we might expect to learn from such examinations of value alike to employer and employed.

Of the immediate importance of heart disease as a source of casualty in industry I am not altogether certain. I would suspect that there is considerable tendency to overestimate its importance. Cases where proven heart disease has been the cause of accident are very rare at best. So far as I know, also, there is no industry which could cause morbid changes in a normal heart. Nor do I believe that either the heart muscle or the valves of a normal heart can be damaged by any exertion or sudden severe strain. Bainbridge (1) says, "There is no evidence that, in a perfectly healthy man, even the most intense exertion produces any harmful effect upon the heart."

Under certain conditions, however, a heart already damaged may develop further changes during employment, resulting in disability or death. A thorough examination of the heart, then, should be a routine procedure, not only at the time of employment, but at regular intervals, when all employees should be reexamined, in industries where health work is possible. Such examinations will be of mutual advantage to the employer and to the employee. To the employer because:

1. There will be very small groups of persons who because of their cardiac

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condition are unfitted for any employment, and should be referred for suitable treatment.

2. There will be a larger number, but still small, who because of limited response to effort are unsuited for the duties which they wish to assume, but may well fill some other position.

3. A knowledge of preexisting heart disease at the time of employment may be of value later. It has happened that compensation has been claimed for an organic heart disease on the assumption that it was due to trauma, or to the effects of the industry. The results of trauma severe enough or of such a nature as to injure the heart are immediate and obvious. As to industry itself, I know of no heart disease which can be associated with any particular industry.

4. It is of advantage that cases of the so-called effort syndrome should at least be recognized.

It is to the employees that the most substantial benefit should accrue:

1. If he has a heart lesion, by fitting him in an occupation suitable to his range of cardiac response.

2. By the diagnosis of the lesion. At present the most substantial contribution that preventive medicine can make to heart disease is its early diagnosis, and recognition of the causal infection. Once that is established, much may be done to prevent further progress, especially by the treatment of the infection if it is still present, or if it is not still present by taking what steps we may to prevent its recurrence with consequent further damage.

The examination should be accompanied by a history covering previous infection and symptoms past or present indicating any cardiac infection, or any insufficiency of the heart in its response to effort. A history of dyspnea on exertion, of edema, or of precordial pain may be of quite as much importance as any finding which may be elicited on examination.

With regard to the examination itself, if it is to be done at all, it should be adequate. The subject should be at least stripped to the waist. Not only should the heart and the aorta be outlined by percussion and palpation, and abnormalities of the heart sounds listened for, but the blood pressure should be taken, the peripheral vessels palpated for any evidence of atheromatous changes, the abdomen examined for signs of passive congestion of the liver or for a spleen enlarged by infection or passive congestion, and the skin examined for petechiae and the extremities for cyanosis or edema. This sounds like a great deal for an industrial examination of one organ, but we learned in our army examinations that if done systematically it could be done adequately and quickly.

Just what may we expect to learn from such an examination?

The small percentage found to have actual cardiac damage may be placed in three main groups with some other classes which we will consider separately:

1. Those showing evidence of anatomic changes in the heart or the vessels, but with no evidence of loss of function as shown by passive congestion or dyspnea, who make a normal response to effort, and in whom there can be found no evidence of a present underlying infection.

2. Those showing evidence of car-

diac damage with loss of function, but who give no evidence of a present infection.

3. Those showing evidence of cardiac damage with or without loss of function, but who do give evidence that the infection which caused the damage is still present and active.

In the first group we have those who give definite evidence of previous cardiac damage, but who are without any evidence of cardiac insufficiency, whose response to effort is normal, and in whom we have ruled out any present infection. Such damage as Lewis (2) has pointed out is a condition and not a disease. It is a scar from something which has passed. If the heart is able to do its work with that condition today it can do so in the future, provided that no further damage is done. Such damage will come first and foremost from infection; either an infection present at the time of examination which we have ruled out in this first group or from the recurrence of the infection which did the damage of which we find evidence. It may be that the anatomic changes, themselves, especially the vascular changes in the valves, render the heart more susceptible to future infection, or it may be that the first infection so sensitized the heart that a mild infection elsewhere, as in the tonsils, which would pass unnoticed in others, may tend to localize in the heart again.

If our health service is to fulfil its duty to the employee it should do what it can to help him to avoid such a recurrence by the care of tonsils, teeth, or other of the many sources of infection, and especially by instruction as to his general health, the avoidance of fatigue and exposure and contact with infection. Just how efficient such precautions may be, is doubtful. The results of our follow-up clinic at St. Luke's Hospital have so far certainly not been encouraging.

Further damage may come from the nature of the lesion itself as is apparently the case in adhesive pericarditis, for example, where the constant traction of the adhesion on the heart muscle may tend to the replacement of the muscle by fibrous tissue. Some physicians consider that mitral stenosis may progress irrespective of infection.

In very few if any hearts of this first group will further damage be incurred because of overexertion. If we are sure of our ground, sure that there is no infection, and sure of the adequacy of the response to effort, I can see no reason why a man whose heart is considered in this group should not be allowed to perform his regular duties. I know of several such patients who have worked for years without further damage, and of others in whom the break when it came was due not to the work, which they carried on successfully, but to further infection.

There is no better test of the response of the heart to effort than the response of the heart to its ordinary duties. The best test as to whether a man can carry on the work desired is, as Dr. Paul White (3) suggests, to try him at it. There is no test exercise, rule, or formula which will replace the individual judgment of the examiner.

The second group yielded by our examination consists of those whose hearts have been damaged to the extent that there are some signs of

cardiac insufficiency, and who do not show a normal response to effort, but in whom we can rule out any present infection. A part of this group will not be suitable for any form of work, and should be directed to the proper channels for treatment. Many of them will be suitable for certain positions, positions which they can fill satisfactorily and without damage to themselves if the work is such that it entails only that effort which the heart can meet readily and easily.

In this group belong cases of mitral and aortic disease whose response to all effort is not normal, but is adequate for certain employments. Many cases of auricular fibrillation may also be placed in this group. A patient with auricular fibrillation, properly instructed in the use of digitalis, may work for years without a break. There are some few cases of fibrillation in which the heart rate remains low with little or no pulse deficit, without digitalis.

In this group again there can be no set formula or rule. It is a matter of individual judgment. And here again the great danger lies in a reinfection.

The third group consists of those who show evident heart disease, but who in addition show evidence of a present infection. As far as employment is concerned, they are ruled out at once. The real onus that falls on the examiner is in their recognition, and in the advice given to the patient.

The most important question which a physician should ask himself on examining a heart is this: Is there, or is there not infection still present? Is there by any chance a mild, subacute endocarditis present smoldering along with few signs of activity and doing slow but constantly progressive damage? The patient with frank endocarditis is quickly eliminated and will not reach the examiner's office. But the patient with a mild, subacute endocarditis may be walking around apparently well, and showing few signs.

Such infection usually occurs in hearts where there has been previous valvular damage, and with an onset so insidious that no clue is given as to the duration of its presence. Such patients may exhibit little or nothing, either subjectively or objectively, to indicate the presence of an infectious process, or the signs may be obvious. It would be of infrequent occurrence to find such patients at the time of examination for employment, but at some time or other they will be found, either on reexamination or on their reporting at the office with complaint possibly of slight malaise, of fatigue on slight effort, of loss of weight, or of some indefinite symptoms. Such cases will come not always from those with previous heart disease, but also from those previously normal.

On examination some pallor may be noticed, due to a secondary anemia. A moderate elevation in temperature, irregular in type, is also invariable, as is an increased pulse rate. The white count is increased. The heart will usually show evidence of valvular lesion. The spleen is in most cases palpable. There may be some clubbing of the fingers. The best evidence usually present at some time during the course is the presence of small petechiae in the skin, most frequently observed in the clavicular region, at the base of the neck, on the forearm, or on the abdomen.

There may be evidence of emboli in the kidneys. Osler's nodes, small, round, red, tender spots on the balls of the fingers or toes may be noted, or a history of such tender spots may be gained from the patient. There may be small, dark red papular lesions in the skin over the dorsum of the foot or the palmar surface of the hand, which are not tender. Where it is possible to obtain blood cultures, a short, green-producing streptococcus will usually be found.

The disease is more frequent than we are apt to credit it with being. Do not think that it is too uncommon to be watched for, for it is not uncommon. It has not the almost invariably fatal outcome that a frank endocarditis has. There are reports of many recoveries, and as we learn to look for it and to diagnose it early, it is probable that our ideas as to its mortality will be still further modified. It is unnecessary to say that such cases should be referred for immediate treatment, and treatment in which the main essentials are absolute rest under favorable conditions, good diet and nursing care, and time—months and months of time.

What we have just said was in reference to heart disease of streptococcic origin. Syphilis presents an even harder problem. We are rarely sure just how active or how quiescent the process is. Left alone, the tendency is to progress. Treatment presents difficulties of its own. The conduct of such treatment rarely falls to the industrial physician, and I shall not consider it here except to call attention to the large number of patients with syphilitic heart in whom disability dates back to the institution of too enthusiastic arsenical treatment. The employment of patients with syphilitic heart or vascular disease is of very doubtful propriety. Untreated, they may go for years, or may progress rapidly; and treated, the progress of the lesion may be arrested, or unchanged, or greatly accelerated. In any case it is the employee with syphilitic disease of the heart or the aorta who is most apt to suffer from overexertion or sudden strain.

Cases of hypertension should be judged by the associated findings, and the history. This will include changes in the peripheral vessels, in the heart itself, and in the kidneys. And again the response to effort is to be weighed against the nature of the employment. Of the so-called essential hypertension, we know too little of what it does or does not mean to consider it separately.

Heart disease consequent upon thyroid changes is too large a subject to be considered in detail. The same canons of distinction apply here as in the cases previously considered.

Another group which will be found during examination are those in whom a history of substernal or precordial pain on effort will be elicited, or the characteristic peripheral radiation of such pain. Or there may be a history of pain somewhere in the peripheral distribution, as the left little finger, or the wrist, or the elbow, or the epigastrium, without the substernal pain. In some, tenderness to the left of the upper portion of the sternum or over the precordium will be found.

In many such cases there will be evidence of syphilitic disease of the heart or the aorta. Just what proportion, will depend on the personnel of

the industry. Occasionally, and especially where the aorta is involved, such pain is part of the picture in the subacute endocarditis. There will be others with definite senile changes in the heart and the vessels, or in whom, without evidence of such changes, the pain is definitely anginal in character.

Anginal pain, while not an index either to the extent or to the presence of cardiac pathology, can never be considered lightly. Many a patient with so-called false angina has died during an attack. Your diagnosis of angina can be established by the history only. By nothing found on physical examination, and by no laboratory finding, can you establish a diagnosis of angina pectoris, or can you rule out its presence. As far as can be demonstrated in many cases, the heart may appear quite normal. Nor can you be guided by the frequency or the severity of the attacks. A man may die in the first or second mild attack, or he may have severe attacks for years. You have no certain method of estimating the prognosis as far as the attacks themselves are concerned. But you do know this —that no employee in whom angina is even suspected should be in a position where his sudden death would endanger others, or where in the event of incapacity he could become involved in moving machinery, or in a severe fall.

While we must be very guarded in our diagnosis of "false angina," and should bear in mind Potain's remark, that he knew of no false diseases but did know of false diagnoses, we must recognize that there are many who complain of precordial pain who have a heart and circulatory system which is quite normal, and who are not to be classified as suffering from angina. As Heatherly (4) comments, such pain is almost invariably precordial, but not substernal. This is especially true of those whom we have learned to classify under the term "effort syndrome" (5). It is what the name implies, a series of symptoms consequent upon effort, but beyond that we know little.

While the symptom-complex termed effort syndrome came into especial prominence in the late war, as it has to a lesser degree in other wars, it does not mean that such cases are at all peculiar to wars or to armies. They are, and always have been, of frequent occurrence in civil life, not recognized as such, but classified as incipient tuberculosis, toxic thyroid, psychoneurosis, etc., and probably most frequently as organic heart disease.

The first and most essential point in diagnosis is that the heart must be anatomically normal. The heart is normal but the autonomic control of the heart is not normal. It is overlabile. It reacts to smaller stimuli, and over-reacts. The respiration and pulse are normal, or nearly so at rest, but an exertion so slight that its effect on the respiration should be unnoticed will cause dyspnea, and instead of a slight acceleration of the pulse we have a marked or an extreme acceleration, which does not return to normal in the usual time. Many will show systolic murmurs. Cyanosis of the extremities may be present. There may be a coarse tremor of the hands, which must not be confused with the fine tremor of thyroid disease. A history of fainting attacks or of giddiness is frequent. There are, in

addition, many other symptoms of autonomic over-reaction, such as perspiration, salivation, etc., on stimuli normally adequate. Precordial pain is frequently complained of, consequent upon exertion or excitement, and occasionally at rest. While usually precordial, it may be substernal; it may radiate as in angina. It may be accompanied by a precordial hyperalgesia.

Pharmacologic tests show that the sympathetic system will over-react to sympathetic inhibition or stimulation, and that the parasympathetics will similarly over-react.

The psychoneurotic element, often present to a tiresome degrèe, we cannot take time to discuss here.

It is probable that in effort syndrome we have a variety of underlying causes. Dr. Osler's terse summary of the etiology says that the fault lies with the germoblast. They fall into Dr. Macfie Campbell's classification of the "constitutionally inferior" (6). Some physical or psychical trauma has brought on a train of symptoms which it would not have brought out in one constitutionally superior. Doubtless in many a mild infection of some sort is present. In the army we saw such cases follow too early a return to duty after what was in some cases only a mild infection or a slight operation. Fatigue would seem to be a factor, the amount of fatigue necessary to bring on the symptoms varying with the degree of predisposition. A similar symptom-complex was seen in aviators who became "stale;" after a period in a rest camp, it entirely disappeared.

I have gone into this class of case further than the title of my paper would warrant, but I have done so because they so frequently are diagnosed as cardiac cases, and because they so frequently voluntarily come to the attention of the examiner.

Conclusion

In conclusion, I wish to make a plea for two types of heart cases. First of all, for the heart case that is not a heart case, for the man who is classified as such because of some extrasystoles, or a sinus arhythmia, or a systolic murmur, or other phenomena not significant of cardiac pathology.

A systolic murmur, as Lewis (2) has pointed out, does not of itself mean anything at all, no matter what may be its quality, when it may be heard, or how it may be transmitted. Premature ventricular contractions are of no significance of themselves, and in ordinary frequency they do not diminish the minute-volume of blood delivered by the heart. Sinus arhythmia may occur in middle life or in the aged, as well as in youth, and never means anything at any time.

Many a man has been given years of worry, or has been made a hopeless neurasthenic, or kept from work or from advancement because of a mistaken emphasis laid on phenomena of no important significance. In general we should take a less dismal attitude toward heart disease. It is not, after all, so terrible if we view it sensibly. Heatherly (4) quotes Dr. Wilkes as observing that there would not be sleeping accommodations in all the London hotels to accommodate those walking the streets of London alive and well, who had been condemned to death by the doctors.

And now as to the other class, those who have really suffered cardiac damage. I have tried to emphasize that the important thing is not the damage that has been done *per se*, but the condition in which the damage has left the heart and especially the heart muscle. This will be shown, not by percussion or auscultation, but in the response of the heart to effort. As I have tried to emphasize, future damage will be done by infection, primarily and almost always, and not by the efforts of industry.

Many patients with heart disease can do a normal day's work, and are doing so, undiagnosed. Others will be capable of only slight effort or of clerical work; but in filling these positions many employers prefer a man with a normal heart to do work requiring more effort. We cannot discuss placement here, but I will refer to the work of Mrs. Sheppard (7), and of Miss Stein (8), and to much other work done under the auspices of the New York Heart Association and similar organizations elsewhere. In many of the larger cities there is a local heart association where co-operation may be secured.

We know very little in regard to the normal involution of heart disease. It is probable that many more cases show more marked anatomic as well as functional improvement than we suppose. We know very little in regard to the course of such cases in industry. What we have learned so far has gone to show that in the absence of infection such patients can successfully fill places in industry. It is only by careful examination in industry and by careful and accurate follow-up that we can learn. For this we must depend most of all on those actively engaged in industrial medicine and surgery.

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THE TOXICOLOGY OF HYDROGEN SULPHIDE*

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HYDROGEN sulphide is one of the noxious gases common in industry; it is nearly as toxic as cyanogen or hydrocyanic acid and its action may be as rapid. In very low concentrations, hydrogen sulphide is readily detected by its characteristic and disagreeable odor. The maximal olfactory stimulus is reached at comparatively low concentrations and beyond this the characteristic odor does not increase in proportion to the rise in concentration. High and rapidly fatal mixtures of hydrogen sulphide and air smell much like hydrochloric acid gas.

HYDROGEN SULPHIDE AS AN IRRITANT GAS

Hydrogen sulphide by its direct action on tissues induces the phenomena of local inflammation and, therefore, is correctly classified as an irritant gas. The large majority of volatile irritants react on contact with the moist surface of the respiratory tract, and the damage to the tissues results directly from the processes of the reaction; the chemical products formed and absorbed are generally harmless. Hydrogen sulphide reacts with moist tissue and local inflammation results, but unlike most irritants, the products, when absorbed, give rise to severe systemic poisoning. Consequently, in most instances of hydrogen sulphide poisoning the symptoms of local irritation are largely obscured by the more striking general poisoning.

It has been shown by the author (1) that the solubility of any irritant vapor largely determines what portion of the respiratory tract is acted upon. Very soluble irritants, such as ammonia or hydrochloric gas, are rapidly taken up by the moist surfaces of the upper respiratory tract. The concentration which reaches the deeper and more delicate respiratory structures is consequently attenuated and the greatest damage done is to the pharynx, the larynx, and the trachea. Hydrogen sulphide is one of the relatively insoluble irritants; one volume of water at body temperature dissolves approximately two volumes of this gas, while one volume of water dissolves, for instance, over 400 volumes of ammonia. Hydrogen sulphide, therefore, extends its action more or less uniformly throughout the entire length of the respiratory tract. The deeper respiratory structures, the atria and the alveoli, suffer the greatest damage; and inflammation of these structures appears as edema of the lungs.

Fatal edema of the lungs can be produced experimentally in animals by

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exposing them for many hours to a concentration of hydrogen sulphide (500 parts per million) insufficient to cause marked general symptoms. In man, also, an occasional fatality occurs from one to three days after the subsidence of acute symptoms and is due to edema of the lungs. The symptoms of lung irritation do not, however, appear in the ordinary clinical case of hydrogen sulphide poisoning either because of the brevity of the exposure or because they are obscured by the systemic action.

The irritant action of hydrogen sulphide is not limited to the respiratory tract but is also exerted on the eyes, especially in persons who are exposed at frequent intervals to low concentrations of the gas. The eyes are directly exposed to the concentration of hydrogen sulphide existing in the surrounding air and are subject to a proportionately great irritation. The first result is an irritative conjunctivitis. Later or in more serious cases, the surface of the cornea appears as if eroded and this is accompanied by characteristic vascular changes, perversions of sight, and, in rare instances, ulceration.

Fate of Hydrogen Sulphide in the Body (2)

The commonly accepted belief that hydrogen sulphide, when inhaled, combines with the hemoglobin of the blood, is incorrect. Sulphemoglobin and sulphmethemoglobin are not formed in the living body by the direct action of hydrogen sulphide. Such hemoglobin compounds may be formed *in vitro* by the action of hydrogen sulphide on blood but the union does not occur until the blood has become completely reduced and then only in the presence of concentrations of the gas far above those which would be instantly fatal if inhaled.

Hydrogen sulphide is oxidized when brought into contact with blood in which the hemoglobin contains oxygen; the blood is proportionately reduced and the hydrogen sulphide destroyed. If fresh hydrogen sulphide is brought to act on the blood after complete reduction has occurred, then, and then only, is a sulphemoglobin compound formed. Only an insignificant deoxidation of the blood in the body is caused by hydrogen sulphide, even when an immediately fatal amount is inhaled, and this reduction does not contribute appreciably to the toxic action of the gas. The oxidation products of the gas are nontoxic and the process of oxidation ends the physiologic action of the absorbed hydrogen sulphide.

There is a persistent, but erroneous, belief that hydrogen sulphide poisoning results in the formation of abnormal hemoglobin compounds. It is based on two observations: (1) Sulphur hemoglobin compounds are formed in putrefying cadavers, and give a greenish color to the flesh and blood, particularly about the intestines; and (2) in persons with the diseased condition of sulphemoglobinemia the blood gives the spectral bands characteristic of the sulphur compounds of hemoglobin. Sulphemoglobin has never been found in the blood of persons who have died from hydrogen sulphide poisoning when the examination was made before decomposition had set in. The formation of sulphur compounds of hemoglobin is a part of the process of decomposi-

tion; the blood becomes completely reduced and the hydrogen sulphide which arises from the bacterial action on protein cannot then undergo oxidation, but combines with the hemoglobin.

The disease sulphemoglobinemia (3) (4) is one of the enterogenous cyanoses; although the blood contains sulphemoglobin, none of the symptoms of hydrogen sulphide poisoning occur. The formation of sulphemoglobin is not the primary disturbance in this disease; the blood contains an abnormal reducing substance which permits the union of the hemoglobin with the hydrogen sulphide even in such small amounts as may be normally found in the intestinal tract. The reducing agent is derived presumably from a nitrosobacillus which inhabits the buccal cavity.

Hydrogen sulphide is an acid substance and, when brought into contact with sodium bicarbonate, forms sodium sulphide. From this fact, some authors have assumed that inhaled hydrogen sulphide is not only converted into sodium sulphide, but is carried in this form in the blood. Such cannot be the case, however, except momentarily, for when sodium sulphide is brought into contact with blood or blood plasma it is hydrolyzed and hydrogen sulphide is liberated. That this hydrolysis occurs in the body is evident from the fact that hydrogen sulphide appears in the exhaled breath of an animal which has received an intravenous or an intramuscular injection of sodium sulphide solution.

When hydrogen sulphide is brought into contact with blood containing oxygen, or is liberated from sodium sulphide placed in the blood, it is oxidized, presumably to sulphuric and related acids, which are neutralized to the sodium salts. Such oxidation products are nontoxic.

During the reaction of hydrogen sulphide with moist tissue or blood there are present hydrogen sulphide, sodium sulphide, and products which arise from the oxidation of the gas. The reaction progresses to the complete oxidation of the sulphide; short of this completion, however, the blood contains diminishing amounts of both sodium sulphide and hydrogen sulphide. It is the free and unoxidized gas in the circulating blood which gives rise to the characteristic toxic symptoms.

Toxic Concentrations of Hydrogen Sulphide

Hydrogen sulphide causes systemic poisoning whenever the concentration inhaled is sufficient to maintain in the blood an amount of the unoxidized gas great enough to exert a pharmacologic action. The hydrogen sulphide which exists in the blood cannot be determined directly by analysis, for the oxidation is of such rapidity that the gas disappears during the time spent in making the necessary manipulations. The concentrations in the respired air corresponding to the various manifestations of the poisoning have been determined, however.

The estimation of the toxic concentrations of hydrogen sulphide is by no means a simple undertaking. A concentration built up in a gassing chamber containing an animal is rapidly decreased through absorption in saliva, urine, hair, metal, etc. Numerous incorrect estimates have consequently found their way into the literature.

By passing a very large volume of air containing an unvarying concentration of hydrogen sulphide through a glass chamber in which a dog was enclosed, and further confirming the maintenance of the concentration by means of repeated analyses, the author has determined the toxic concentrations as presented in Table 1. The figures given are in complete agreement with those found by Lehmann (5).

TABLE 1.—THE TOXIC CONCENTRATIONS OF HYDROGEN SULPHIDE

CONCENTRATION OF HYDROGEN SULPHIDE IN AIR			SYMPTOMATOLOGY
Mg. per Liter	Parts per Million	Per Cent.	
0.14 to 0.21	100 to 150	0.01 to 0.015	Symptoms of local irritation after many hours of exposure.
0.28 to 0.42	200 to 300	0.02 to 0.03	Causes local irritation if inhaled for one hour and slight general symptoms if inhaled longer.
0.70 to 0.97	500 to 700	0.05 to 0.07	Causes local irritation and slight systemic symptoms within one hour. May cause death after exposure of several hours.
1.0	900	0.09	Causes systemic symptoms in less than thirty minutes. May cause death in less than one hour.
1.7	1,500	0.15	Causes death after fifteen to thirty minutes of exposure.
2.0	1,800 and over	0.18 and over	Causes almost immediate death through paralysis of breathing.

Systemic Poisoning by Hydrogen Sulphide

The entire systemic action of hydrogen sulphide is on the nervous system. In very low concentrations the action of the gas is in general that of mild depression, both physical and mental. In concentrations of approximately 1,000 parts per million and over in the air breathed, the action passes from depression to the stimulation which characterizes the acute forms of poisoning. The stimulating action is not limited to any one fraction of the nervous system.

The behavior of respiration is of the utmost importance for it is the abolition of this function which leads directly to death in acute hydrogen sulphide poisoning. The response elicited in the heart and the skeletal muscles through the action of the gas on the nerves which supply them, though striking, has less significance.

Action of Hydrogen Sulphide on Respiration (6)

Hydrogen sulphide is to the highest degree a noncumulative poison; the response of respiration to inhalation

of the gas is immediate, and proportional to the concentration breathed. Respired air containing less than 1,000 parts per million (0.1 per cent.) has a negligible influence on respiration. Above this concentration active hyperpnea is induced within a few minutes. With continued inhalation the hyperpnea increases and soon terminates in respiratory failure. With a concentration of 1,500 parts per million (0.15 per cent.) the course of events is the same except that the reaction is more intense. With concentrations of 2,000 parts per million (0.2 per cent.) and over there is little preliminary hyperpnea, and breathing is paralyzed after a breath or two of the contaminated air. In such concentrations the victim falls to the ground as though struck down.

The stimulating action of hydrogen sulphide on respiration appears to be directed on the pulmonary endings of the vagus nerve. Animals in which this nerve has been cut tolerate concentrations of hydrogen sulphide between 1,000 and 2,000 parts per million without marked respiratory effects. When the concentration passes the 2,000 parts per million mark, however, respiratory paralysis occurs in these animals just as it does in those in which the vagus nerve has not been cut.

The chemical regulation of respiration is not directly affected by hydrogen sulphide in the circulating blood or by the oxidation products. Although these substances are acid in nature, the total amount of acid thus added to the blood is too small to affect appreciably the hydrogen-ion concentration.

Asphyxia develops as a result of the paralysis of breathing induced by high concentrations of hydrogen sulphide. The heart, however, continues to beat for several minutes after respiration has ceased. If the subject can be induced to breathe by artificial means, or if artificial respiration is maintained until the hydrogen sulphide in the blood is oxidized, normal respiration soon becomes reestablished and the subject suffers little serious consequence. Natural breathing is never reestablished spontaneously following paralysis of respiration by high concentrations of hydrogen sulphide. The rapidly progressing oxygen deficiency caused by the cessation of breathing slows the oxidation of the sulphide in the blood and also brings the respiratory mechanism to a subnormal state.

The failure of respiration induced by concentrations of hydrogen sulphide between 1,000 and 2,000 parts per million is of a type distinct from the paralysis discussed above. It follows the excessive breathing which results in an elimination of carbon dioxide from the body and the development of an acute acapnia. Such overventilation is followed by a compensatory period of respiratory inactivity, known as apnea, which persists until the normal amount of carbon dioxide has reaccumulated in the body. The hyperpnea resulting from hydrogen sulphide is followed by a similar apnea. The stimulation of respiration by the gas is opposed by the removal of the normal stimulus to breathing, for the hydrogen-ion concentration of the blood is reduced, so that a point is finally reached at which the depression of the respiratory center becomes effective. Breathing is then stopped, no more hydrogen sulphide is inhaled, and that in the body is

oxidized. If the depletion of the body's supply of carbon dioxide has not progressed too far, this substance may reaccumulate and reestablish respiration before the respiratory mechanism has become damaged by the asphyxia occurring as a result of cessation of respiration. If spontaneous recovery does not occur and artificial respiration is not instituted, death from asphyxia follows. In some cases the gassed subject may reestablish respiration spontaneously while still in the contaminated atmosphere; and in this event the cycle described above is repeated but with a decreased resilience of the respiratory mechanism and a lessened likelihood of recovery from the second paroxysm of hyperpnea and apnea.

Action of Hydrogen Sulphide on the General Nervous System

The action of hydrogen sulphide is not limited to any one part of the nervous system. In severe poisoning convulsions, muscular rigidity, and jactation form a characteristic part of the general picture but contribute little toward the fatal outcome. The reaction of the skeletal muscles is not from central stimulation, for it occurs in the lower limbs even after the cord is severed in the cervical region (statements in the literature to the contrary, notwithstanding).

The heart is slowed by the action of hydrogen sulphide, which is probably exerted through the vagus nerve. A marked bradycardia may develop after the inhalation of concentrations insufficient to affect the respiration or cause convulsions. In spite of the cardiac slowing, the action of the heart continues otherwise unimpaired for several minutes after respiration has failed in the more acute forms of poisoning.

The nerves which supply salivary and sweat glands are stimulated by hydrogen sulphide. A profuse flow of saliva and cold perspiration may follow exposure to concentrations of the gas insufficient to produce the more acute forms of poisoning.

Chronic Hydrogen Sulphide Poisoning

Prolonged exposure to low concentrations of hydrogen sulphide is generally believed to result in a chronic form of poisoning. This is characterized by local irritation of the eyes and the respiratory tract, bradycardia, cold sweats, lassitude, digestive disturbances, headache, and, in some cases, skin eruption. Although these symptoms are somewhat indefinite, there appears to be little question that the repeated and prolonged inhalation of hydrogen sulphide in concentration as low as 100 parts per million (0.01 per cent.) may cause local irritation and depression of the nervous system, not unlike that following a prolonged course of bromides.

Prophylaxis of Hydrogen Sulphide Poisoning

Every effort should be made to guard against contamination of the air by hydrogen sulphide. As stated above, the sense of smell is not a reliable indicator for the concentration of the gas in the air.

Complete protection against the inhalation of hydrogen sulphide is afforded by suitable masks which are

now on the market. For those repeatedly exposed to small amounts of the gas the eyes must be carefully protected. The eye lesion is entirely due to local irritation on the surface of the cornea and the conjunctiva, and is not, as is sometimes supposed, a result of inhaling the gas. Air-tight goggles, either alone or as part of a mask equipment, give satisfactory protection if properly and conscientiously used. Goggles of this type, however, are uncomfortable and prone to cloud with moisture, and frequently are poorly fitted.

When the air of a building is contaminated by hydrogen sulphide, forced ventilation or some other means of rapidly changing the air may be employed to reduce the dangers of poisoning. Forced ventilation, however, is expensive and if the volume of liberated sulphide is variable, it is frequently ineffective.

The more severe cases of hydrogen sulphide poisoning commonly occur in men entering sewers, from leaks in the chambers or pipe lines of the soda apparatus used in the Leblanc process, and from leaks in oil stills. Under these conditions the only preventive is the enforced wearing of protective masks for those liable to exposure.

Resuscitation from Acute Hydrogen Sulphide Poisoning

From the discussion of the physiology of hydrogen sulphide poisoning, it is apparent that the resuscitative measures after acute hydrogen sulphide poisoning are directed entirely to the maintenance of respiration. If the gassed subject can be brought to uncontaminated air before the heart has ceased to beat (four to eight minutes), and if manual artificial respiration is instituted immediately and continued without interruption, there is every probability that life will be saved, and that except for the possibility of subsequent pulmonary edema the after effects will be negligible. Artificial respiration in every instance should be given by the Schäfer or prone pressure method. It should not be performed if the subject is breathing; and it should be at once discontinued when spontaneous breathing returns. Mechanical devices for performing artificial respiration should be avoided and full reliance placed in the manual method. In its relation to artificial respiration, hydrogen sulphide poisoning resembles electric shock; to be of any benefit the administration must be immediate and when so performed is usually lifesaving; a delay of even a few minutes is fatal.

The mixture of oxygen and 5 per cent. carbon dioxide now extensively employed in resuscitation after carbon monoxide asphyxia (7) (8) (9) is beneficial in hydrogen sulphide poisoning. The carbon dioxide in this mixture materially aids in reestablishing spontaneous breathing and the oxygen helps to relieve the anoxemia. The mixture should be given with the so-called H-H Inhalator which is designed for this purpose. If possible the inhalation should be started during the period of artificial respiration and should continue for a short time after the return of normal breathing. The fact must not be overlooked, however, that inhalation for those who have stopped breathing is useless unless manual artificial respiration is given at the same time.

Pathology of Hydrogen Sulphide Poisoning

Hydrogen sulphide poisoning has no distinctive pathology. The autopsy findings of acutely fatal cases are simply those of asphyxia. In the occasional case in which death is delayed for a day or two, evidence of edema of the lungs may be found.

Neither hydrogen sulphide nor any combination of this substance with the blood pigment or blood alkali is ever found in the body at early autopsy after hydrogen sulphide poisoning. If there is a delay in performing the autopsy, however, blood pigment combined with hydrogen sulphide may be found in abundance. The bluish-green color of this sulphur compound is particularly noticeable in the vessels surrounding the intestines. The formation of sulphemoglobin or sulphmethemoglobin under these circumstances is entirely a postmortem change, and is not in any way indicative of a previous exposure to hydrogen sulphide.

Conclusions

Hydrogen sulphide is both extremely toxic and also irritant. It causes severe local irritation of the eyes and may induce pulmonary edema. The more severe irritant effects are, however, usually obscured by the symptoms of acute systemic poisoning.

Hydrogen sulphide is rapidly oxidized in the body. The oxidation products are nontoxic. In this, as in the intensity of toxicity, it compares with cyanides. Inhaled hydrogen sulphide forms no combination with, nor does it in any way alter, the hemoglobin of the blood.

In acute poisoning death results from respiratory failure. With concentrations below 0.1 per cent., respiration is little affected; with concentrations of 0.1 to 0.2 per cent., severe hyperpnea is induced and this terminates in apnea vera; with concentrations over 0.2 per cent., respiration is paralyzed without a preliminary hyperpnea. Breathing may be resumed spontaneously after the apnea but never (unless assisted by artificial respiration) after the paralytic form of respiratory failure.

The heart continues to beat for several minutes after respiratory failure. During this time manual artificial respiration (Schäfer method) will reestablish breathing. Inhalation of oxygen containing 5 per cent. carbon dioxide is beneficial during and for a short time after the period of artificial respiration.

The prophylaxis of hydrogen sulphide poisoning consists in wearing suitable masks and goggles or keeping the contamination of the air at a low level by means of forced ventilation.

The author expresses his thanks to Professor Yandell Henderson for comments and criticisms.

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OBSERVATIONS IN BLAST-FURNACE GASSING*

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BLAST-furnace gas is by far the most frequent cause of gas poisoning in the steel industry. It is an odorless gas of smoke gray color, with a peculiar sweetish taste. Our analyses show its composition to be as follows:

	Per Cent.
Carbon monoxide	25
Carbon dioxide	12
Oxygen	6
Hydrogen	2
Nitrogen	55

The variations in percentages and in constituents seem, in my opinion, to indicate that blast-furnace gas, illuminating gas, producer gas, and gas from automobiles should be considered separately in the causation of complications or sequelae following gassing.

In a period of twelve years' work in industrial medicine, during which time I have treated approximately 1,200 cases of gassing, I have had no deaths, complications, nor sequelae following mild or severe gassing. All of my cases have been acute; no case of chronic poisoning has as yet been reported to me. In all fatal cases death has occurred at the place of exposure. Contrary to the experience of others, I have not found any pulmonary complications such as pneumonia, bronchitis, or edema of the lungs, nor have I seen a case with subsequent brain, nerve, or blood sequelae or complication. A great majority of the men who have been gassed are still in our employ and quite a number represent repeated gassings.

Our illness records for the past two years show that among blast-furnace employees there was less lost time due to pulmonary disease than among other lines of employment. The reason for this I am unable to state.

The treatment which I have employed during the past twelve years consists of a hypodermic injection of camphor in oil (3 grains in sterile olive oil) and the application of heat to the body, usually by an electric pad. In conjunction with this, especially in severe cases, I have used the H-H Inhalator since its introduction. The combination of oxygen (95 per cent.) and carbon dioxide (5 per cent.) which it supplies is vastly superior to oxygen alone.

My experience with the camphor in oil is that it acts as a twofold stimulant—to the respiratory center and to the vasomotor center. Respiration is accelerated and deep breathing results. By stimulating the vasomotor center I am enabled to relieve the chilliness and cold of which the patients complain. Mental depression and dulness are relieved in the majority of cases. The most troublesome complaint that I have found is the so-

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called "gas headache." This I have been able to relieve with calomel, following a saline and large doses of sodium bicarbonate (20 to 30 grains every two hours).

I am submitting this report in the hope that some investigator will run a series of experiments to ascertain whether or not camphor in oil has a direct influence in preventing pulmonary complications in cases of gassing. My findings have been as follows:

1. Uniformly good results.
2. Absence of complications and sequelae.
3. Quick and complete recovery.

INDUSTRIAL POISONING BY INHALATION*

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Translated by J. W. S. Brady, M.D.

[This paper is one which would ordinarily be covered in the Abstract Section of THIS JOURNAL. The experience of the editors has, however, indicated that there is still a widespread lack of appreciation of inhalation as the principal portal of entry for industrial poisons. It is consequently considered appropriate to print the paper in its entirety.

The reader will understand from the general character of the statements involving matters of pathologic physiology that the author regards much of the material presented as open to controversy.—*Ed.*]

INTRODUCTION

INDUSTRIAL poisoning by inhalation, as might be surmised from the term, includes all states of acute or chronic poisoning where the toxic substance enters the organism through the respiratory passages in the course of work.

The industrial intoxications that can occur under these conditions are many, since the respiratory tract is accessible not only to gases, fumes, and vapors, but to solid substances distributed in the air in the form of dust. The number will appear even greater if we consider how many substances, both solid and liquid, harmless enough in their natural state, are changed in the course of manufacture by such physical processes as fusion, boiling, and evaporation, and are then readily introduced into the body in the form of gases, fumes, or dust.

No one denies that gases, fumes, and vapors enter the system through the lungs. There is, however, some difference of opinion as to whether it is possible for them to penetrate the organism and produce their harmful effects without the participation of the lungs. As far as dusts are concerned, both radioscopy of the living and examination of the cadaver reveal the presence of pneumonokoniosis, which means that dusts have succeeded in passing the pulmonary alveoli. It may be argued that pneumonokoniosis can occur through some other route—for example, the digestive tract—but this has never been proved. Even admitting the possibility of a gastrointestinal pneumonokoniosis, the pneumonokoniosis of respiratory origin will still be the usual form. In order to reach the pulmonary alveoli, however, dust must overcome many obstacles set up by the air passages—the tortuosities of the nasal passages, the centrifugal activity of the vibratory cilia, the mucous secretion of

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the glands throughout, and the protective reflexes of nervous origin, such as coughing, sneezing, and bronchial spasm. With continued exposure these defenses gradually lose their efficacy, until the ingress of foreign substances with the respired air occurs easily and freely.

The absorption of gases and vapors takes place through the delicate alveolar wall which separates the external environment from the capillary network of the blood. This is a simple process of diffusion according to Dalton's law. Absorption, therefore, depends on a difference in the partial pressures of the gases contained in the blood and those contained in the atmospheric air—the two phases being separated by capillary walls and alveolar epithelium. When accidental gases are mixed with air, each gas of the mixture tends to diffuse into the blood in proportion to its different concentration at each of the contact surfaces. Diffusion ceases and absorption is complete when equilibrium is reached between the vapor tensions of the several gases dissolved in the blood and the partial pressures of these gases in the adjoining atmosphere. The blood in circulation then carries the absorbed gases to all parts of the organism.

The mechanism of the absorption of dusts is more complex. They reach the lungs after passing the nasal labyrinth, the mouth, larynx, trachea, and bronchi. It is not in the scope of this article to consider ingestion through the digestive tract of substances passing the upper respiratory tract. Dust, after reaching the parenchyma of the lung or on its way thither, may be dissolved by the body fluids and immediately absorbed and introduced into the circulation; or, if it remains undissolved, it either is absorbed by desquamating epithelial cells, or, passing through the pulmonary epithelium, enters the supporting connective tissue where it may occasion an inflammatory process with the exudation of leukocytes from the blood vessels and the lymphatics.

Toxic substances once in the blood are brought into contact with all the tissues, and, since the circuit of the body requires but twenty-three seconds, it is easy to understand the rapid distribution of poisons throughout the organism.

The discussion of industrial poisoning by inhalation is best considered under two aspects: poisoning from gases, fumes, and vapors; and poisoning from dusts.

Effects of Gases, Fumes, and Vapors on the Respiratory Tract

Certain gases and fumes entering the respiratory tract can produce a general toxic action without harm to the respiratory tract. These are the purely toxic gases. Other gases which exert a general toxic effect may produce changes in the respiratory system which vary in the extent and in the permanence of the damage. These are the gases with mixed effect —generally toxic and locally irritant. Finally there are a number of gases which on contact with the respiratory tissues act with such violence as to make any general toxic symptoms they might cause of secondary im-

portance. These are the irrespirable gases.

Irrespirable Gases.—The irrespirable gases are so called because they cannot be breathed even in slight concentration in the air without serious harm to the respiratory organs. Their action is chiefly, if not entirely, local. The first effect is a reflex spasm originating in the mucous membranes lining the respiratory tract—the nose, mouth, larynx, and bronchi. It occurs in the form of sneezing, coughing, attacks of suffocation from closure of the glottis, and spasm of the diaphragm. There are even more serious reflex reactions, such as pneumocardiac reflexes with disturbances of the heart beat or cardiac syncope, and pneumopneumonic reflexes with disturbances, possibly cessation, of respiration. As a result of the penetration of irrespirable gases, mucus and other glandular secretion is greatly increased, causing intense lacrimation, diffuse bronchial catarrh, pulmonary edema, often pulmonary consolidation which is lobular (although sometimes lobar) in type and may be fibrinous, hemorrhagic, or purulent. The effect on the mucous membranes and the alveolar walls is an inflammatory process more or less intense to the point of necrosis. Types of irrespirable gases are: sulphur dioxide, sulphuric acid fumes, nitrous fumes, and the vapors of hydrochloric and hydrofluoric acids, of ammonia, and of chlorine.

Gases of Mixed Character.—Gases, fumes, and vapors of mixed character (generally toxic and locally irritant) have this characteristic that, although their passage through the respiratory tract is not harmless, the changes produced do not endanger life but permit the substance inhaled and absorbed further to unfold its toxic properties. To this group belong hydrogen sulphide, dimethyl sulphate, diazomethane, acetic acid, acrolein, bromine, formaldehyde, amyl alcohol, acetaldehyde, ethylaldehyde, chromic acid, phosgene, turpentine, pyridine, phosphorus, para-phenylenediamine, etc. All these substances in the form of gas cause more or less irritation, produce coughing, sneezing, congestion of the mucous membranes, and bronchial catarrh. Most of them act throughout the respiratory tract; some, however, attack certain definite places. Phosphorus, for example, produces necrosis of the lower jaw sometimes occurring several weeks after entrance of the worker into the factory, sometimes delayed for twenty years, and sometimes never occurring at all. At first the gums are swollen and carious teeth fall out; then dental abscesses and fistulae are formed, and bony necrosis with the formation of sequestra results. Sometimes the necrosis spreads to include the whole jaw. In general it is the lower jaw that is affected but cases involving both jaws are described. Necrosis may extend from the lower to the upper jaw, to the nasal bones, and to the base of the skull. Phosphorus necrosis affects individuals with carious teeth. It seems that phosphorus facilitates the spread of the process to the alveoli and the medullary cavity of the bone where the micro-organisms of the decayed tooth transplant themselves and cause simple osteomyelitis, leading to rarefaction. Para-phenyl-

enediamine has a similar specific effect in that it can produce attacks of true essential asthma. All these substances naturally produce their general toxic effect when absorbed and distributed to the body tissues subsequent to the local inflammatory reaction.

Toxic Gases.—Finally, there are the toxic gases and vapors. These pass through the respiratory tract without any trace of their passage through its various parts. Their action is general; its effects are found in the various organs and systems according to the coefficient of distribution of the absorbed substance. Gases, vapors, and volatile substances that are purely toxic are numerous. No list would be complete because the ceaseless activity of industrial progress tends toward a constantly increasing utilization of all materials and an increased danger in their employment by modification of their physical state in the course of manufacturing.

Effects of Dusts on the Respiratory Tract

As has been stated, dusts obtain admission to the system through the respiratory tract, but as not all are poisonous they can be classified as dusts that are indifferent or inert, and dusts that are chemically active or toxic.

Only the latter—that is, dusts that are chemically active or toxic—are concerned in the present discussion. These are known to reach the alveoli of the lungs and may pass through their walls to attain the glands of the hilum and continue on through the lymph channels to the parenchyma of the great glandular organs. As particles of dust accumulate in the lymph glands they occasion a series of degenerative processes. The first step is a connective tissue hyperplasia; the next a true sclerosis which, through interference with the pulmonary lymph flow, results in injury to the lung tissue and in retention of the dust in the interstitial spaces. As a reaction to the stimulus of dust particles, young connective tissue elements appear that contract and cause sclerosis of the surrounding lung tissue. The end is not only a diminution or even a suppression of the respiratory function of the affected part, but from the impaired circulation a nutritional disturbance also results which leaves the tissue an easy prey to bacterial infection. The mucous membranes are not indifferent to the action of dusts. Microscopically, a moderate congestion is visible; microscopic examination reveals more or less serious inflammatory lesions of the lining of smaller and larger bronchi, a thickening of the alveolar walls with the epithelial cells swollen and often desquamating into the lumen of the alveolus where pus and blood cells are usually found.

Clinically, symptoms occur in agreement with the anatomic lesions just described: obstinate cough, sputum more or less abundant and blood tinged, rhonchi and râles distributed throughout the respiratory tract—in short, the symptomatology of a diffuse chronic bronchitis, frequently with periods of acute exacerbation. In the course of time the cough and bronchitis may produce more or less extensive pulmonary

emphysema with its accompanying train of symptoms and disorders.

Dusts, so long as they retain their solid state, cannot exert a general toxic effect, even though they are reduced to the finest powder. In order to produce a general effect they must pass into a state of solution. Dusts that cannot be dissolved by tissue fluids may cause a pathologic or clinical picture of pneumonokoniosis; they may cause local inflammatory reactions, but they can never be responsible for functional disturbances or anatomic alterations in distant organs. Only in a state of solution can they be absorbed and thus distributed throughout the whole organism. Some chemically active or toxic dusts are easily dissolved; others less so. Soluble dusts for the most part change their physical state during the passage from the nose or mouth to the alveoli of the lung; slightly soluble dusts change their state with difficulty during their journey through the air passages—only in the interstitial tissue of the lung, in the subpleural or peribronchial lymph glands, are they accumulated, modified, and transformed by the tissue fluids. This is the result either of a purely chemical contact action or of fermentation processes.

Dusts that are easily soluble do not, as a rule, induce in the respiratory tract the changes previously described. By their rapid solution, absorption, and distribution they produce disturbances of a general rather than of a local nature. Excepted from this, of course, are those dusts which dissolve with a formation of acid or alkali, or which, on solution by hydrolysis, liberate their irritating constituents such as acids and alkalies. Under such conditions in addition to the general disturbances there are local manifestations of irritation, such as corrosion or ulceration. Sometimes, as for example following the inhalation of chromates, perforation of the nasal septum takes place. Dusts that are dissolved with difficulty remain for a long time stored up in the respiratory organs and the associated lymph glands. They produce there the above-mentioned local changes. Later, depending on the time needed for solution and absorption, the general phenomena occur.

General Toxic Effects of Gases, Fumes, and Dusts

Having discussed briefly the changes produced on the respiratory organs by gases, vapors, and solid particulate matter penetrating the organism, a consideration of the general toxic effects, the remote action of these same substances, is in order.

The general action of such substances entering the body by inhalation is no different from that produced by the same substances absorbed through other routes—gastric, cutaneous, or parenteral. The poisons once absorbed, through whatever channel, are taken up by the blood and carried to the various tissues, into which they diffuse according to the coefficient of distribution. Some poisons are excreted immediately; others become fixed in the different tissues and are later given up more or less rapidly to the blood which takes care of their elimina-

tion in the same or in a modified state. The period intervening between the absorption and the elimination is of the greatest importance. As a rule, the quicker the excretion, the less harmful is the action, and *vice versa*. Some substances are quickly removed; others require weeks and months. In the latter case they do not continue to circulate freely in the blood but are retained by certain tissues, especially the liver, the bone marrow, the nervous centers, and the blood elements, from which little by little they are withdrawn and excreted.

By way of explanation of the behavior of different individuals toward poisons, it has been suggested that the elimination is more rapid in those persons in whom nutrition is more active and in whom the excretory organs are more nearly perfect, functionally and anatomically.

On the Excretory Organs.—The excretory paths are the kidney, the skin, the gastro-intestinal tract, and the lungs. In general, soluble substances are eliminated through the urine and through sweat; other substances, either undissolved or combined with protein, are excreted through the bile and the feces; volatile substances, through the lungs. This mechanism of excretion is not without variation. The same substance may be eliminated in various ways. Sometimes when its usual excretory organ is inadequate or poorly functioning, a substance may be expelled through another route of excretion—a fact which shows the ability of the organism to reject through the best means at its disposal the harmful substances attacking it. The kidneys are certainly one of the most important emunctories. Most of the mineral salts, dyes, and coloring materials pass out in this way. Elimination varies according to the substances concerned. Some are removed rapidly and completely; for others, renal excretion is more prolonged; and in many cases elimination does not occur until the offending substance has undergone transformation.

In the digestive tract excretion occurs through the saliva, the gastric juice, the bile, and the intestinal secretions. Sometimes the gastro-intestinal tract represents an alternative route for the kidneys. The poison passing through it may produce functional disturbances in the form of vomiting or diarrhea. In this way are excreted many of the insoluble poisons and those which combine readily with body albumins; in the bile are found mostly those poisons that are retained by the liver, as well as those that combine with hemoglobin, or possess hematolytic power.

The lungs not only serve essentially for the excretion of gases and volatile poisons, but may also possess more complex duties. Recent studies have tended to show that in addition to their respiratory function the lungs exert a protective action in the nature probably of a glandular enzyme. The lung acts on certain substances which are brought to it by the venous blood and which it cannot excrete. This action, tending to lessen the activity of the poison, is closely allied to the respiratory function, since obstructing the entrance of air

lessens the protective power of the lung.

The passage of poisons through the various excretory organs is not without influence on their histologic and functional integrity. The type of lesion produced varies according to the concentration of the poison, the duration of elimination, and the selectivity of the action. The sudden arrival of powerful poisons in high concentrations may produce serious changes, resulting in suppression of function or even in death. The lesions observed in the kidneys are degenerative—albuminous or fatty degeneration of the tubular epithelium, which in swelling compresses the cortical vessels and produces an ischemia aggravating the effect of the degeneration. If the lesions are not fatal, regeneration and repair follow, or else regression and cicatrization. When the poisons arrive gradually, vascular and interstitial lesions develop. The poison produces its changes in the remotest vascular branches, and, passing the vessel walls, stimulates the connective tissue around the glomeruli and tubules to respond with formation of new connective tissue elements. These lead to a final shrinkage and scar formation. The vascular and interstitial lesions once established lead to reciprocal aggravation. Clinically, the picture is that of parenchymatous and chronic interstitial nephritis.

In the digestive tract lesions have been observed in the oral mucous membrane in the form of stomatitis. The first effect is often salivation, followed by a sense of discomfort or irritation like that due to a foreign body. The mucous membrane of the gums appears swollen and whitish with an accumulation of proliferating pavement epithelial cells. The teeth appear raised and elongated. Later the mucosa erodes and ulcerates. The free margin of the gums is beefy and grayish, bleeds easily, and is covered with pultaceous material of a grayish and gangrenous appearance. The breath is fetid, and mastication is painful.

In poisoning with lead or bismuth, it is usual to find along the free margin of the gums, especially about the lower incisors and about carious teeth, a special pigmentation. Similar deposits are often found on the inner (mucous) surface of the cheek at about the level of the molars or the premolars. Other pigmented spots are found not infrequently along the whole digestive tract. They are thought to be due to a secondary sulphide action on the eliminated metal. It is not uncommon in some intoxications to find a swelling of the parotid gland—the result of a chronic inflammatory glandular hypertrophy.

The digestive disturbances produced by poisons reaching the stomach through the blood are well known. Subjectively the patients complain of loss of appetite, acute thirst, a tendency to nausea, vomiting, gastric meteorism, and gastric hyposecretion. In the gastric mucosa in the cadaver can be found more or less well-marked signs of fatty degeneration. This involves both the superficial and the glandular epithelium. The mucosa appears pale, swollen, and opaque. Microscopically, the epithelial cells show at

first a cloudy swelling; later, the presence of fatty droplets. By degrees their structure is lost until desquamation occurs. In severe cases there are signs of acute catarrhal gastritis. The mucosa is red and swollen and overlaid with a coat of mucus. Microscopic examination shows hyperemia and increased secretion of mucus, swelling and degeneration of the epithelial cells, increase of leukocytes in the glandular connective tissue, and abundant migration of leukocytes through the epithelial surface.

Symptomatically, from the intestine arise paroxysmal crises of pain which are localized over more or less extensive abdominal areas (colic), with obstinate constipation or profuse diarrhea. Frequently there are duodenal ulcers associated in all probability with toxic changes in the blood vessels. In the glandular mucous membrane it is easy to find signs of a fatty or sclerosing enteritis. From the liver occur symptoms of a proliferative interstitial parenchymatous hepatitis (hypertrophic cirrhosis). Poisons eliminated through the bile may produce an inflammatory reaction in the bile passages.

The absorbed poisons are carried by the blood into contact with all the tissues of the body so that functional disturbances or anatomic changes may occur anywhere. In order to act, the poisons must combine with the tissues. Inasmuch as this combining power is not uniform for all organs but varies according to the coefficient of distribution, it happens that certain symptoms frequently occur earlier or in a severer form in the course of a certain intoxication, and thus offer valuable aid in differential diagnosis. Every poison absorbed may have a special as well as a general symptomatology. In other words, many poisons produce special changes manifested by particular symptoms.

Space is too limited to discuss the symptomatology of each intoxication, and such discussion would but repeat the textbooks. It seems more timely to group under various headings the functional disturbances and the lesions produced, with the understanding that rarely does a poison act on a single organ. Many substances considered but recently to be poisonous exclusively for one part of the body have, by the newer methods of investigation, been shown to possess a much more extensive and complex action.

Poisons act on the functions of organs in two ways—they accelerate, or they paralyze. In general, minute doses produce an exaggeration of the function of the affected organ; large doses, conversely, a diminution. For instance, in minute quantities lead stimulates the action of the intracellular ferments; in larger quantity it paralyzes their activity. The action of alcohol is similar, in a different field; at first it produces exhilaration (a state of excitation) and later, depression, corresponding to a paralysis.

Even from the anatomic standpoint, the two phases of hypo-activity and hyperactivity can be shown. If the toxic dose is small, phenomena of anatomic cellular hyperactivity occur; if the dose is larger, cellular degeneration of parenchymal tissues and regression leading to sclerosis are found.

Overwhelming intoxication may cause fatal degeneration of cell elements and, consequently, severe disturbance of function.

There are substances which by influencing the activity of the intracellular ferments produce a marked effect on the metabolism. Such action corresponds to that of the so-called catalyzers. If added to macerated tissue material kept aseptically at a temperature of 37° to 40°C., variations in the phenomena of autolysis can be produced—either acceleration or retardation, according to the quantity of poison present. Corresponding to this action verified *in vitro* is a similar action observed *in vivo*, in the sense that small amounts of these poisons accelerate and accentuate the disintegrative processes in the depths of the tissues, while large quantities retard or completely paralyze these processes. In the first case, nitrogen elimination through the urine is increased; in the second, it is diminished. There are few investigations that show this action of the common industrial poisons, and of these few the majority have been carried out in the Milan Clinic.

Substances active in these metabolic changes of acceleration or retardation are the salts of mercury, lead, arsenic, iron, manganese, gold, cobalt, aluminium, magnesium, potassium, sodium, copper, strontium, nickel, cadmium, silver, and phosphorus. The depressant action of some of these is so great as to produce cachexia. Besides the general action, there is specific action on particular ferments. Present-day knowledge covers in this respect but few substances. Among them are lead, which *in vitro* as *in vivo* heightens the activity of these ferments concerned in the formation of uric acid, and carbon dioxide, which conversely acts on the ferments that from the products of cleavage and decomposition resynthesize uric acid. Such phenomena explain the increase of uric acid in the blood of the saturnine and of the gouty manifestations in these patients, as well as the uricaciduria and uricacidemia in persons breathing air with a high percentage of carbon dioxide.

Electrolytes of sodium and potassium seem to have a catalytic action on other enzymes, especially the amylolytic. Perhaps a similar action is caused by carbon dioxide, which *in vivo* can produce a temporary glycosuria. Whether this glycosuria is associated with changes in the islands of Langerhans, or with modified activity of the starch-splitting and sugar-splitting ferments, is uncertain. The chapter of special catalytic activities is among the most interesting in toxicology, for advances in this field would explain a number of phenomena which, still unexplained, we accept as a result of observation.

On the Blood.—Many substances possess an affinity for the blood. Some may circulate freely or in combination in the blood without causing a change in its chemical or morphologic composition. There are, however, a number of substances which alter its constitution. From this point of view, the hemotoxic substances can be divided into two great groups: protoplasmic poisons and poisons of the morphologic element.

Protoplasmic poisons can diminish the coagulability of the blood, or

can abolish it entirely for a time. This is shown by the hemorrhagic tendency of internal or hollow organs, and of external or internal mucous membranes, and by hemorrhagic suffusions—ecchymoses and petechiae of the skin, of the mucosae, and of the endothelium of the most diverse organs. This is characteristic of the action of the salts of sodium, copper, iron, manganese, cobalt, and nickel, and of the action of benzol and benzine. This action explains the intestinal hemorrhages in phosphorus poisoning. Some ascribe this anticoagulating action to a stable compound which the poisons form with fibrinogen, destroying its coagulating power. Others suppose a platelet insufficiency.

The opposite effect is produced by other substances which increase the coagulability of the blood and make it dense and viscous. Alcohol and carbon dioxide are the only substances known to act in this way except some of the hematolytic poisons, such as lead, mercury, carbon monoxide, arsine, nitrobenzol, and aniline.

The chief poisons of the morphologic elements affect the resistance of the red blood cells; of a few which increase it, formaldehyde is the only one worthy of mention. Those decreasing the resistance of the red blood cells—the hematolytic poisons—are numerous. *In vitro*, lead, mercury, and silver, in salts or in colloidal solutions, reveal this property in setting free hemoglobin from the red cells. *In vivo*, they produce a marked anemia and a disturbance of the hemoglobin balance. The liberated hemoglobin is excreted partly through the kidneys, partly through the liver where it causes an increased production of bile, and shows itself in highly colored feces, sometimes in jaundice, and sometimes in hematoporphyrin, urobilin, or hemoglobin in the urine. In addition to lead, mercury, and silver, may be included copper, carbon monoxide, arsine, stibine, carbon disulphide, phosphoric anhydride, aniline, benzol, nitrobenzol, picric acid, and nitrites.

In some intoxications, certain structural peculiarities have been discovered in the red blood cells. In nitrobenzol poisoning one finds in the red cells minute corpuscular bodies described by Heinz, Ehrlich, and others. More remains to be learned about these bodies, although most investigators consider them a form of degenerative color change of the blood pigment. In lead poisoning basophilic granulations are found in the red cells in the earliest cases. Remarkable diagnostic importance has been attributed to these granules. Basophilic stippling is, to be sure, present in other morbid conditions, especially in pernicious anemia, in the leukemias, and in severe secondary anemia. If found in a lead worker, however, one can confidently assert that in that individual the poison has begun its harmful work. Many interpretations have been put forward as to the significance of these granules; at present the opinion of the majority is that they represent a stage of maturation of the normal red blood cells.

In contradistinction to these substances producing erythropenia are others causing erythrocytosis. Poisoning from phosphorus, carbon

monoxide, and arsenic can produce a polycythemia. Under certain circumstances the characteristic picture of the polycythemia anemica of Weber may ensue, characterized by an increase in the number of red cells with a diminution not only of the color index but also of the total quantity of hemoglobin.

Certain poisons combine with hemoglobin, forming a more or less stable compound and hindering the reversible reaction with oxyhemoglobin.

$$O\,Hb \rightleftharpoons Hb + O$$

From this results an anemia of the tissues. Carbon monoxide acts in this way to produce carboxyhemoglobin. The blood in carboxyhemoglobinemia retains its ruddy color in the veins. Microscopically it appears normal, but on spectroscopic examination it reveals its characteristics. The absorption bands are unchanged by such reducing agents as ammonium sulphide or Stokes' solution. A similar type of change results from nitrogen dioxide, acetylene, and ethylene. Hydrogen sulphide produces sulphmethemoglobin with an absorption band in the red, and the whole blood appears blackish. In cyanide poisoning, a stable compound, cyanhemoglobin, is formed which in the spectroscope shows two absorption bands near the violet end of the spectrum. Carbon dioxide reduces the oxyhemoglobin to reduced hemoglobin, an unstable compound which gives up its carbon dioxide in the presence of oxygen. Methemoglobin is produced by numerous other substances: chromates, nitrobenzol, nitroglycerin, amyl nitrite, nitrotoluol, nitroxylol, dinitrophenol, nitrochlorobenzol, nitrophenol, trinitrophenol, nitrophthalein, azobenzol, aniline, toluidine, paranitraniline, para-phenylenediamine, etc. When they do not destroy the red blood cells these substances have little pathologic effect on the blood.

There is also a series of poisons which increase or reduce the number of white corpuscles. In general, any toxic substance provokes a cellular reaction in the blood. In certain acute intoxications this reaction is a leukocytosis—for example, in poisoning by dimethyl sulphate, nitrobenzol, arsine, lead, mercury, alcohol, and carbon dioxide. In certain chronic conditions, especially where there is anemia, the reaction is a leukopenia. There are substances exerting a special lytic action on the white blood cells. Chief of these is benzol, which on account of this property has been elevated to a drug for the treatment of leukemia. In benzol poisoning leukopenia is among the first symptoms to appear; the same is true of poisoning from antimony. In intoxications where the white blood cells are destroyed uric-aciduria and uricacidemia from the nuclear material of the white cells may be present.

The cytologic formula also may be modified. Mononucleosis is found in poisoning by silver, benzol, and carbon dioxide; a neutrophil polynucleosis in those intoxications causing leukocytosis; an eosinophil polynucleosis in poisoning by carbon monoxide, phosphorus, mercury, nitrobenzol, benzine, picric acid, acetanilide. The white cells may contain abnormal granules, especially sudan-

ophil granules in poisoning by phosphorus, antimony, and arsenic.

There are substances that act on the platelets to produce an excessive number of gigantic platelets—for example, lead, carbon monoxide, and aniline oil. Together with this change goes an increased viscosity of the blood. Other substances, such as benzol, reduce the number of platelets, and in consequence there results a diminution of the viscosity of the blood, followed by hemorrhages—a picture resembling thrombocytopenia.

In closing the section on blood changes it might be well to add that in the circulation in many anemic states due to poisoning immature cells of the red and white series are found. The presence of these immature elements is dependent either on a functional hyperactivity of the blood-building organs, or on a stimulation of the bone marrow and the lymphatic apparatus by the poison, or on the indirect action on the blood-forming organs caused by the anemia itself, since it is well known in anemic conditions that in most cases the body tends to restore the altered blood constitution.

On the Nervous System.—The majority of toxic substances are able to produce disturbances or lesions in the nervous system. Some combine with the nervous tissues in an unstable manner and are readily given up to the blood to be eliminated; others remain fixed for some time and are excreted slowly. Still other substances, independent of the duration of the combination, can produce histologic changes, especially in the nerve cells. Only in this last case are the functional disturbances produced permanent; in the first mentioned cases the disturbed functioning persists only as long as the poison remains fixed in the nervous system.

Even a brief sketch of the various clinical pictures produced by poisons in the nervous system would require a textbook, so great is the number of nerve poisons and the variety of symptoms in the various regions affected. Some poisons are, so to speak, paralyzers of the whole central nervous system. First of all the psychic volitional centers are affected; later the functioning of the vital centers in the medulla are arrested. Among such poisons are chloroform, ether, ethyl chloride, aniline, nitrous oxide, methane, ethylene, carbon monoxide, carbon dioxide, the alcohols and aldehydes, benzol and benzine, carbon disulphide, and certain compounds of arsenic and of hydrocyanic acid.

Nerve poisons could be divided according to the part of the nervous system primarily affected: poisons of the cerebral cortex, of the basal ganglia, of the cerebellum, of the medulla oblongata, of the spinal cord, and of the peripheral nerves. Such a division would, however, be highly artificial since most substances according to their dosage and rapidity of absorption may attack either a single one of the various divisions of the nervous system or several divisions simultaneously with a polymorphous picture. Some of the very poisons which in large doses paralyze the whole cerebrospinal axis may, in smaller doses, attack only one definite segment. Clinical studies may

reveal some predominating action. From action on the cerebrum there may result cephalalgia, insomnia, psychic disorders, maniacal attacks, and convulsion; from action on the cerebellum—dizziness, lack of muscular co-ordination, and staggering gait; from action on the medulla—dyspnea and palpitation, slow breathing, bradycardia, even respiratory arrest and cardiac syncope, Biot's or Cheyne-Stokes' respiration, nausea, vomiting, convulsions; from action on the spinal cord—disturbances of motility and sensation. The same substances acting on various segments or on the same segment may produce at one time an excitation, at another time, a paralysis. In addition to transitory functional disturbances, the same poison can produce histologic changes resulting in permanent impairment of function.

What has been said is enough to indicate the complexity and the infinite variety of clinical syndromes produced by nerve poisons. Among the multiplicity of nervous symptoms must not be forgotten the disorders of the peripheral nervous system in the form of paresis, paralysis, tremors, disturbances of sensation, trophic disturbances, neuritis, and muscular atrophies. In the production of these lesions the same substances and the same poisons are involved.

Paralysis may be general or local, and its extent depends on the amount of poison absorbed. There may be quadriplegias, hemiplegias, or paraplegias. In localized paralyses the extensor muscles of the joints are affected first and most frequently; but it is not possible to speak of a true selective action on certain muscle groups or certain nerves. Lead, for example, which seems to have a predilection for the muscles innervated by the radial nerve, attacks other muscle groups. Usually the earliest sign of paralysis is in the extensor muscles, but this rule is by no means constant or absolute. Some substances, chief among which is mercury, produce a more or less diffuse tremor. Still others cause toxic meningitis. The poison reaching the meninges is able by irritation to produce a congestion. From this there results an increased intraspinal pressure, clouding of the cerebrospinal fluid, an increase in albumin and globulin, and the presence of polymorphonuclear leukocytes without morphologic changes. The spinal fluid is sterile, aseptic; both the negative culture and the integrity of the white cells confirm this. Clinical symptomatology is that of the ordinary septic meningitis.

In certain intoxications lesions of the sensory organs are observed. The eyes are most frequently affected in the form of amblyopia, amaurosis, retinal changes, or optic atrophy. This is common to poisoning by lead, alcohol, nitrobenzol, and carbon disulphide. Deafness, as well as disturbances of smell, taste, etc., has been reported in poisoning by carbon disulphide.

On the Heart.—Some poisons are able more or less quickly to affect the cardiac activity. This may occur directly through degenerative processes arising in the muscle fibrils, as happens in the cellular elements of other tissues. From this arise symptoms of myocarditis. If the degenerative process involves the

papillary muscle or the myocardium about the valve openings, there may be true murmurs from these anatomic foci at the mitral or the tricuspid valves. Poisons may affect the autonomic centers of the heart, the sinus node, the auriculoventricular node, the bundle of His, the intrinsic and extrinsic nerves, producing disturbances of the excitation, the contractility, and the tonicity of the myocardium. Many substances, moreover, influence the action of the heart through the central nervous system.

On the Blood Vessels.—The blood vessels are not immune from poisons which modify their caliber and by acting on the blood pressure affect the heart. Examples of vasoconstrictive poisons are lead, antimony, and aniline. By causing hypertension they result in hypertrophy of the left ventricle. The vasoconstriction is caused by direct action on the vessels or by indirect action through the nervous system. There are also a number of substances with vasodilator action, substances that act by paralyzing the vasoconstrictors. These are the nitrates, nitroglycerin, benzol, the alcohols, benzine, the aldehydes, chloroform, ether, and the cyanides. By lowering the blood pressure they produce an acute insufficiency of the heart and the kidneys. The clinical picture is cyanosis, visceral congestion, slowing of venous circulation, and the phenomena of uremia. Finally, there are a number of substances which have a sclerosing action on the blood vessels, such as lead, antimony, alcohol, and aniline. The favorite point of attack is usually the coronary arteries, the cerebral vessels, or the aorta; the arteries of particular organs or the peripheral arteries in general are affected. The end-result is total or partial arteriosclerosis, with symptoms varying according to the organs involved.

On the Liver.—The liver is one of the organs most frequently affected by intoxications. The lesions most readily produced are fatty degeneration and a productive parenchymatous hepatitis. Many substances cause angiocholitis and, from the disturbed biliary circulation, jaundice. Jaundice may result also from the action on the liver parenchyma of poisons such as phosphorus and tetrachlorethane. Other poisons act indirectly in liberating the hemoglobin of the red cells which passes through the liver and forms bilirubin. This group includes the hematolytic poisons such as arsine, nitrobenzol, and aniline.

On the Glands of Internal Secretion.—Little is known about the effect of poisons on the functions of the glands of internal secretion. Lesions of the islands of Langerhans and glycosuria have been described following carbon monoxide poisoning. Autopsy showed marked hypertrophy of the suprarenal capsules, and an increase of adrenaline in the blood, suggesting a hyperactivity of the adrenals. Following the increased function was a state of hypofunction with the syndrome of hypo-adrenalism. Inhalation of bromine decreases the lipoids and reduces the chromaffin substance of the capsules. Chlorine, phosgene, and acrolein produce occasionally congestion and more or

less well-marked degeneration in both zones of the suprarenals.

Still more uncertain is the knowledge of the other internal secretory glands. As far as the thyroid is concerned lead, arsenic, phosphorus, and alcohol produce sometimes stimulation, sometimes a sclerosing action on the tissue of the gland, depending on the duration of the poisoning. In regard to function it is certain that iodine has a stimulating effect and phosphorus and arsenic a paralyzing effect.

On the Bladder.—One more condition remains to be mentioned which occurs with considerable frequency in chemical factories where colors, especially aniline colors, are made. This is tumor of the bladder. Apart from statistics nothing is known of the specific action of aniline and aniline compounds in producing vesical tumors. Some suggest that they are caused by the amido bodies which by oxidation act on the epithelial elements of the bladder and stimulate proliferation. The tumors found are benign or malignant. Their situation varies. In general, they occupy the region beside the ureteral orifices, sometimes the trigon, sometimes the space anterior or posterior to it. They may occur on the anterior wall but rarely in the neck of the bladder.

On the Genital Organs.—Modern experimental research has shown the passage of many toxic substances from mother to fetus through the placental circulation. From this it is clear that industrial poisoning of the mother may exert its harmful effect on the offspring. The fetus may react unfavorably to the toxic condition of the mother, or the poison passing through the placenta to the fetus may produce conditions unfavorable to its further development; hence the frequency of abortion, stillborn children, and infants of poor vitality. The following industrial poisons have been shown to pass from mother to fetus: lead, phosphorus, mercury, alcohol, ether, carbon disulphide, benzine, copper, antimony, trinitrotoluol, tritol, benzol, and picric acid.

Some of these substances in addition exert a harmful action on the function of the sex organs. Lead causes dysmenorrhea and metrorrhagia. In chronic mercurialism the menstruation is delayed, amenorrhea occurs associated with chlorosis. During menstruation, hemorrhages are frequent. In alcoholism, there is precocious cessation of the menses and anaphrodisia. In carbon disulphide poisoning, there has been reported genital atrophy, irregular menses, and loss of sensitiveness to a point of indifference. In addition, many substances passing in the milk during lactation are a source of danger to the baby.

The male function also is affected unfavorably by some industrial poisons which seem to affect the condition of the offspring. The history is given of a painter whose case was followed by the Milan Clinic:

1868.....Born.
1885.....Began work as a painter.
1888–1891...Military service.
1891.....Returned to painting.
1892.....First signs of lead poisoning.
1893.....Married.
1894.....First abortion.
1895.....Baby A born.
1895.....Second abortion.

1898.....Baby B born.
1899.....Wife died of pulmonary tuberculosis.
1900.....Second marriage.
1901.....Baby born; died of meningitis.
1903.....Baby born; died of bronchopneumonia.
1904.....Lead colic.
1907.....Recurrence of lead colic.
1907.....Baby C born.
1910-1911...Baby A and baby C at the Clinic. The girl A was much retarded in development; the baby C had marked signs of rickets, scrofula, and hernia.

This family picture is striking but it is not widely different from that of many other families where the father is affected by lead poisoning.

Preventive Measures

Fortunately, not all industrial poisons affect the workman handling them. In comparison with the vast number of poisonous substances in use in industry, the number of cases of industrial poisoning is small. This is due to the introduction and the employment of various technical protective measures. Prevention of poisoning by inhalation is not a problem of the individual. The worker breathes the atmosphere of his environment and if this is contaminated he has no other protection than to leave his environment. It is, therefore, incumbent upon the industry to employ the measures necessary to free the workroom as much as possible from hazards arising from the manufacturing processes. Preventive measures must be employed against the diffusion of gases and fumes and against dusts.

As far as gases, fumes, and vapors are concerned, it is obvious that the minimal toxic quantity and the quantity readily tolerated by all workers should be known. For various gases the limits as far as they are known are shown in Table 1. It should be the duty of the employer to have the figures determined for other substances for which the limits are not known. When the employer wishes or finds it convenient, he can always control the amount of poisonous substance in the surrounding air and can aim at atmospheric purification. The ideal way to prevent fume poisoning is to prevent diffusion of the fumes; in cases where this is impossible, measures can be employed for their removal. Workrooms should be airy and spacious, and furnished with sufficient windows for a rapid change of air; if necessary, in addition to natural ventilation, there should be artificial exhausts, situated high or low according as the gases to be removed are lighter or heavier than air. When not in use, the workrooms should be closed to workmen and the air should be changed. The manufactured product, if it exhales gases or fumes, should be removed from the workroom. Even more strict precautions should be taken in those parts of the plant where gases which are either irrespirable or powerfully toxic develop. These manufacturing processes should take place in the open air, as is now done in some modern factories.

What has been said of gases, fumes, and vapors applies equally to dusts. The ideal way is to prevent their development or at least to remove them by well-placed exhausts before they diffuse into the air. At times diffusion is prevented by humidi-

fication of the atmosphere and of the material employed. If such measures are not sufficient to prevent the entrance of dusts into the respiratory tract, recourse should be had to

of the manufacturing processes in the plant, and should know all the toxicologic facts about the substances employed, the clinical syndromes which they produce, and the technic

TABLE 1.—MINIMAL TOXIC DOSES OF VOLATILE POISONS

NAME OF VOLATILE POISON	CONCENTRATION			
	Rapidly Fatal for Man and Animals	Causes Severe Symptoms in ½–1 Hour	Can Be Tolerated without Harm ½–1 Hour	Tolerated for Several Hours
Hydrochloric acid	.....	1.5–2%	0.05–0.1%	0.01%
Sulphur dioxide	.....	0.4–0.5%	0.05–0.2%	0.02–0.03%
Prussic acid	0.3%	0.12–0.15%	0.05–0.06%	0.02–0.04%
Carbon dioxide	30%	60–80%	40–60%	20–30%
Ammonia	.....	2.5–4.5%	0.3%	0.1%
Chlorine and bromine	1%	0.04–0.06%	0.004%	0.001%
Iodine	.....	.....	0.003%	0.0005–0.001%
Phosphorus trichloride	3–5 mg.	0.3–0.5 mg.	0.01–0.02 mg.	0.004 mg.
Phosphoretted hydrogen	.....	0.4–0.6%	0.1–0.2%	.....
Hydrogen sulphide	1–2%	0.5–0.7%	0.2–0.3%	0.1–0.15%
Benzine	.....	.....	15–25 mg.	5–10 mg.
Benzol	.....	.....	10–15 mg.	5 mg.
Carbon disulphide	.....	10–12 mg.	2–3 mg.	1–1.2 mg.
Carbon tetrachloride	300–400 mg.	150–200 mg. per liter	25–40 mg. per liter	10 mg.
Chloroform	300–400 mg.	70 mg.	25–30 mg.	10 mg.
Carbon monoxide	.....	2–3%	0.5–1%	0.2%
Aniline and toluidine	.....	.....	0.4–0.6 mg.	0.1–0.25 mg.
Nitrobenzol	.....	.....	1.0 mg.	0.2–0.4 mg.

respirators (gas masks). It must be borne in mind that these do not give absolute protection; even the best masks permit about 10 per cent. of the suspended dust to pass, and, moreover, because of the annoying hindrance to respiration, they are not kindly received by the workmen.

Such hygienic measures do not attain complete efficacy without the services of a plant physician. In order to fill such a position successfully, a physician should have not only a sound general medical knowledge but also a special knowledge

of discovery of the earliest symptoms. A physician of these attainments should be a good judge of the desirability of employing any person in those processes where special requirements are needed to resist harmful substances; he should be able to detect in time those affected; and should advise the factory management in hygienic matters. The author is convinced from his personal experience that the plant physician can be a most effective aid in the suppression of industrial poisoning. Devoto has justly observed that

CORRECTION

(To be bound in Volume 7 of the JOURNAL OF INDUSTRIAL HYGIENE, opposite page 140)

Following the publication of the translation of Dr. Preti's article on "Industrial Poisoning by Inhalation," in the March issue of THIS JOURNAL, the attention of the editors was called to the fact that the table appearing in the translation was seriously in error. This table in its original form, by K. B. Lehmann, appears in Rudolf Kobert's Kompendium der praktischen Toxikologie zum Gebrauche für Aerzte, Studierende und Medizinalbeamte, Fifth Edition, Stuttgart, 1912, page 45. The original error was apparently made when the table was translated from the German to the Italian, and consisted in rendering as percentages the figures followed by the mathematical sign °/₀₀. This error makes practically all the figures given as percentages ten times too high. A correct translation of Lehmann's table is as follows:

TABLE (VII) OF THE SMALLEST AMOUNTS OF NOXIOUS FACTORY GASES WHICH ARE STILL POISONOUS AND THE AMOUNTS WHICH IN ANY CASE ARE ENDURABLE

DESIGNATION OF VOLATILE POISONS	CONCENTRATIONS WHICH			
	Are Quickly Fatal for Man and Animals	Cause Illness Dangerous to Life in ½–1 Hour	Are Endurable without Serious Disturbances for ½–1 Hour	Cause only Minimum Symptoms with Several Hours' Action
Hydrogen chloride (hydrochloric acid)	.....	1.5–2°/₀₀[1]	0.05–0.1°/₀₀ at the most	0.01°/₀₀
Sulphur dioxide	.....	0.4–0.5°/₀₀	0.05–0.2°/₀₀	0.02–0.03°/₀₀
Hydrogen cyanide (hydrocyanic acid)	about 0.3°/₀₀	0.12–0.15°/₀₀	0.05–0.06°/₀₀	0.02–0.04°/₀₀
Carbon dioxide	30°/₀	about 60–80°/₀₀	40–60°/₀₀	20–30°/₀₀
Ammonia	.....	2.5–4.5°/₀₀	0.3°/₀₀	0.1°/₀₀
Chlorine and bromine	about 1°/₀₀	0.04–0.06 °/₀₀	0.004°/₀₀	0.001°/₀₀
Iodine	.....	.....	0.003°/₀₀	0.0005–0.001 °/₀₀
Phosphorus trichloride	3.5 mg.	0.3–0.5 mg.	0.01–0.02 mg.	0.004 mg.
Phosphine (phosphoretted hydrogen)	.....	0.4–0.6°/₀₀	0.1–0.2°/₀₀	.....
Hydrogen sulphide	1–2°/₀₀	0.5–0.7°/₀₀	0.2–0.3°/₀₀	0.1–0.15°/₀₀
Benzine	.....	.....	15–25 mg.	5–10 mg.
Benzol	.....	.....	10–15 mg.	about 5 mg.
Carbon disulphide	.....	10–12 mg.	2–3 mg.	1–1.2 mg.
Carbon tetrachloride	300–400 mg.	about 150–200 mg. in 1 liter	about 25–40 mg. in 1 liter	about 10 mg.
Chloroform	300–400 mg.	70 mg.	25–30 mg.	about 10 mg.
Carbon monoxide	.....	2–3°/₀₀	0.5–1.0°/₀₀	0.2°/₀₀
Aniline and toluidine	.....	.....	0.4–0.6 mg.	0.1–0.25 mg.
Nitrobenzol	.....	.....	1.0 mg.	0.2–0.4 mg.

[1] Attention is called to the mathematical signs °/₀ and °/₀₀; 1°/₀ = 1%, and 1°/₀₀ = 0.1%.

THE JOURNAL owes this correction to Dr. R. R. Sayers of the United States Public Health Service, and is grateful for his assistance in correcting a serious error.

"if law still hesitates to legislate the physician into industry, the plant owner himself could with profit create such an office."

Another method of prophylaxis is by substituting for the toxic substances, where possible, other substances less poisonous or even harmless. Thanks to such measures some dangerous processes have become already almost innocuous. For example, there is the mirror industry where mercurialism has disappeared with the elimination of quicksilver; the match industry where phosphorus necrosis is rare since white phosphorus has replaced red phosphorus; the rubber industry where the less toxic naphtha is being substituted for benzol. Some day paint manufacture and painting will become hygienic when the recommendations of the Geneva Conference concerning white lead are carried into effect.

The employer should have the greatest interest in making his plant hygienic if for no other reason than for the greater freedom it allows him in selecting workmen, and the consequently lessened expense. Perhaps for this reason he would be willing to accept regulations which apply generally and are not excessive, which would help to lessen or prevent occupational poisoning.

In Italy, except in some progressive municipalities, there exist no laws regulating industry in the aforesaid sense. There is an industrial hygiene code prepared by a group of eminent authorities among whom it is pleasant to record Professor Devoto, but this code forms no part of the state laws and regulations.

Another measure which would succeed in an indirect way in reducing occupational poisoning would be insurance against occupational disease. This social provision, although freely discussed, has not yet been introduced in Italy. Beside the spirit of justice which would welcome such insurance along with the accident insurance which is now in force, the application of such a measure would tend to a reduction of occupational poisoning as has been the case with accidents. It is the author's opinion that the principle of compensation for industrial disease should be straightway included in the law, beginning with a risk limited to a definite list of a few diseases. Experience will gradually permit an extension of the original list as has already been done in France, England, and Switzerland. The employer, alone, for reasons of equity should bear the expense; the state and the workman should not contribute toward it.

Diagnosis and Treatment

Diagnosis of industrial poisoning is not always easy. Some intoxications present well-defined clinical pictures and almost certain symptoms that permit a diagnosis, as, for example, poisoning by lead, phosphorus, mercury, arsenic, benzol, and carbon disulphide. On the other hand, there are certain toxic states that are not easy to differentiate. In such cases aid must be sought of the laboratory for the examination of the blood and the urine; an accurate history of the patient's illness, and a knowledge of his trade and of the substances handled are required. It is well to remember the words of Bernardino

Ramazzini: "Medici munus plebeios curantis est interrogare quas artes exerceant."

The treatment of poisoning is solely symptomatic; there are no antidotes for the occupational intoxications. The principal treatment is to remove the patient from his work at the first signs of poisoning—thereby removing the *causa peccans*, and permitting the organism with supportive treatment to recover. Elimination of the poison through the various emunctories should be assisted by all the means that modern therapy possesses—diaphoresis, diuresis, and purging. In fulfilling these two fundamental conditions, medication to influence those organs whose function is affected should not be omitted.

Conclusion

The following conclusions can be drawn from the foregoing:

1. The respiratory apparatus is a path of entry to the organism for most industrial poisons. Through it not only the gases, fumes, and vapors enter but the dusts as well. Many substances which in their native state as solid or liquid cannot be inhaled may undergo, during the process of manufacture, changes of physical state which allow them to penetrate the organism readily through the respiratory tract. Industrial poisoning by inhalation is relatively frequent.

2. According to whether the action is on the respiratory tract, on the respiratory tract and the general health, or exclusively on the general health, gases and fumes can be classified as: (*a*) irrespirable gases; (*b*) gases which are locally irritant and generally toxic; and (*c*) toxic gases.

3. The pulmonary lesions produced have no special characteristics except those of the ordinary inflammatory processes.

4. Toxic dusts are either readily soluble and rapid in action, or they dissolve slowly and before producing general effects lead to pneumonokoniosis, a state of chronic bronchitis, and essential pulmonary emphysema.

5. Industrial poisons when absorbed produce the same effect as when they are introduced into the system in other ways. The toxic action is closely dependent on the method of elimination. Although the poisoning is general, nevertheless certain organs retain greater or lesser quantities according to the coefficient of distribution. Hence, certain functions are more affected.

6. The diagnosis of industrial poisoning through inhalation is not always easy. The confirmation of certain intoxications requires laboratory aid as well as a knowledge of the occupation and of the substances handled.

7. Preventive measures against the inhalation of poisons are not individual measures. They should be undertaken by the employer and should aim to prevent the diffusion of gases, fumes, and dusts, either through properly placed exhausts or, where powerful poisons are employed, by carrying on the process out of doors. Another hygienic measure is the substitution, where possible, of less toxic substances.

8. Finally, good results in pre-

venting industrial poisoning will attend the introduction of compulsory insurance against occupational diseases, legislation which for many reasons should be introduced as soon as possible.

BOOK REVIEWS

INTERNATIONAL CLINICS. Volume III. Thirty-Fourth Series, 1924. Cloth. Pp. 292 and index. Philadelphia and London: J. B. Lippincott Company, 1924.

This volume contains five articles on public health and hygiene of which one, "Progress in Dental Hygiene," by R. W. Leigh, D.D.S., is of distinct importance to the industrial physician. Leigh's paper consists of a review of the pathology and etiology of dental caries followed by a logical discussion of the means of control. Since the etiology of the condition is but poorly understood the author seems abundantly justified in his warning against indiscriminate so-called prophylactic work by "dental hygienists" who may destroy natural tooth surface by too vigorous abrasive cleansing.

Another article of interest to industry is contributed by J. J. Walsh and is entitled "Health Examinations and Some Unfortunate Effects." Walsh gives a number of instances in which ordinary types of medical examination have resulted in suggestions to the patient which have become the basis of nervous disorders gravely detrimental to health and efficiency. Perusal of Dr. Walsh's most readable article will result in wise precaution upon the part of the industrial physician whose duty calls for preventive examinations at periodic intervals. The suggestions in the paper apply particularly to the handling of executives and the more important members of industrial staffs. —*Cecil K. Drinker.*

INTERNATIONAL CLINICS. Volume IV. Thirty-Fourth Series, 1924. Cloth. Pp. 294 and index. Philadelphia and London: J. B. Lippincott Company, 1924.

This volume contains two rather general papers relating to industrial medicine, one on "Periodic Health Examinations" by E. B. Edie, M.D., and another on "The Practical Application of Industrial Medicine" by L. E. Cofer, M.D. The first of these papers contains little of value. The second gives a review of recent progress in industrial hygiene and closes with a brief summary of compensation regulations in New York.—*Cecil K. Drinker.*

THE EFFECTS OF INANITION AND MALNUTRITION UPON GROWTH AND STRUCTURE. By *C. M. Jackson,* M.S., M.D., LL.D., Professor and Director of the Department of Anatomy, University of Minnesota. Cloth. Pp. xii, 616 with 117 illustrations, 13 tables, bibliography, and index. Philadelphia: P. Blakiston's Son & Co., 1925.

To students of nutritional disorders this book presents a mine of information in a form that is readily accessible. While a more critical point of view might seem desirable the author has purposely avoided this and states in the preface " . . . . a systematic review of the subject of inanition seems desirable, especially from the viewpoint of morphology. The pres-

ent work will therefore include not only the results published by the author and his coworkers during a decade of research in this field, together with a considerable amount of unpublished material, but also a comprehensive review of the widely scattered data in the literature concerning the morphological effects of inanition in all living organisms. While an adequate critique in so vast a field is impossible, it is hoped that even a brief survey of the literature will be of interest and service. Especial care has been taken to make the bibliography as complete and accurate as possible, although errors and omissions are unavoidable."

The book is divided into three parts: I. Plants and Invertebrates; II. Vertebrates; and III. Conclusion, Tables, and Bibliography. Part II constitutes the greater part of the book and consists of separate chapters each devoted to the effect on the body as a whole, integument adipose tissue and mammary gland, skeleton, teeth, musculature, brain, spinal cord, peripheral and nervous system, visual apparatus, heart and blood vessels, blood, lymph and lymphatic glands, spleen, thymus, alimentary canal, liver, pancreas and salivary glands, respiratory tract, urinary tract, male and female reproductive tracts, suprarenal glands, thyroid and parathyroid glands and the hypophysis.

The method of presentation and very limited amount of critical discussion make the book rather dull reading even to one interested in the field. For reference, however, the book has a wealth of information, presenting as it does a condensed view of a wide variety of work. A great many data are tabulated at the end and there is an excellent bibliography of 108 pages.

It is to be hoped that Professor Jackson may be tempted to bring to fruition a second volume representing his own mature views on the many phases of this very important field.—*Lawrence T. Fairhall.*

ANNOUNCEMENT OF MEETING OF THE AMERICAN ASSOCIATION OF INDUSTRIAL PHYSICIANS AND SURGEONS

The American Association of Industrial Physicians and Surgeons will hold their annual scientific meeting in Altantic City on May 25 and 26, at Hotel Traymore.

The program promises to be an unusually interesting one and a large attendance is expected. Members desiring hotel accommodations should make arrangements at the hotel of their choice.

A. W. Colcord, M.D., *Secretary and Treasurer*
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